

CASE REPORT

Rare renal tumor – mucinous tubular and spindle cell carcinoma

ALINA GRIGORE¹⁾, LIANA TOMA²⁾, M. STOICEA¹⁾, M. DINU³⁾,
 CARMEN ARDELEANU¹⁾

¹⁾Department of Pathology,
 "Victor Babeș" National Institute, Bucharest

²⁾Department of Pathology

³⁾Department of Urology
 Central Military Hospital, Bucharest

Abstract

We report a rare case of renal tumor – mucinous tubular and spindle cell carcinoma in a 65-year-old man. The tumor, located in the right kidney, was well circumscribed. Microscopically, the tumoral proliferation was composed of cuboidal cells arranged in tubules, with abrupt transition to spindle cell morphology in a myxoid stroma. Because of the favorable prognosis with this type of tumor, mucinous tubular and spindle cell carcinoma must be differentiated from papillary renal cell carcinoma, especially the variant with sarcomatoid dedifferentiation.

Keywords: spindle cells, mucinous stroma, renal carcinoma, low grade.

Introduction

Mucinous tubular and spindle cell carcinoma is a rare and unique kidney tumor, first described in 1997 by MacLennan GT *et al.*, named at that time “low-grade collecting duct carcinoma” [1]. It was first recognized as a specific entity in the *World Health Organization* 2004 classification, with less than 100 cases reported [2] until now. It is a low-grade polymorphic renal epithelial neoplasm with mucinous tubular and spindle cell features [3]. Its origin is unknown, possibly in the loop of Henle or in the collecting duct epithelium. Although showing a spindle cell (low-grade sarcomatoid) component, it appears to be a tumor with a less aggressive biologic behavior [4]. Most tumors have been reported in females (M:F 1:3–4), with age ranges from 17 to 82 years (mean 53 years) [2, 3]. Typically, they present as asymptomatic masses, often found by accident on ultrasound [3, 5, 6]. Occasionally, they may present with flank pain or hematuria [3].

Before being recognized as a distinct histopathological entity, mucinous tubular and spindle cell carcinoma was often misdiagnosed as aggressive and highly lethal variants of renal cell carcinoma, most frequently the sarcomatoid variant. One of the main features of this tumor is the good prognosis. Therefore, since the histopathological features can often be misleading, the diagnosis should include a phenotypic analysis of tumoral cells using immunohistochemical markers that allow a better characterization and a differential diagnosis from more aggressive renal cell carcinoma variants. We report a new such case of tumor in a 65-year-old man.

Materials and Methods

An asymptomatic 65-year-old man, with no history of personal or familial disease, was subjected to a routine ultrasound examination performed by his personal physician, which revealed a 63/38.7 mm solid mass in the superior pole of the right kidney. He was directed to and admitted in the Department of Urology, in the Central Military Hospital in Bucharest, for further evaluation. Renal function tests were normal. A computed tomography scan of the abdomen revealed a 51.5/47.2 mm well-circumscribed right renal mass protruding into the renal pelvis. No abnormality of the usual blood tests was detected. Based on these results, a surgical intervention was scheduled. Right large nephrectomy (surgical excision of the kidney, the adrenal gland and the perirenal fat) by anterior transperitoneal incision was performed.

The surgical excision piece containing the tumor was sent to the Department of Pathology in the same hospital for detailed analysis. Tissue samples were fixed in 10% formalin, processed histologically and embedded in paraffin blocks. Sections were cut at 4-μm thickness, stained with Hematoxylin–Eosin, Alcian Blue and Periodic Acid–Schiff (PAS) stains for the initial microscopic evaluation.

The case was later referred to the Department of Pathology in “Victor Babeș” National Institute in Bucharest for immunohistochemical testing. An indirect bistadial technique was performed with a polymer based detection system (EnVision⁺ Dual Link System-HRP, Dako, Carpinteria, CA) according to the manufacturer's instructions. Paraffin sections were deparaffinized,

rehydrated and rinsed in PBS pH 7.4. Retrieval with cooking in specific buffer was raised in microwave oven (Whirlpool) at 800 W for 5 minutes, and 440 W for 10 minutes. The cases were tested by immunohistochemistry (IHC) using monoclonal antibodies against cytokeratin 7 (CK7) (clone OVTL 12/30, Dako, dilution 1:50), epithelial membrane antigen (EMA) (clone E29, Dako, dilution 1:50), vimentin (VIM) (clone V9, Dako, dilution 1:50), carcinoembryonic antigen (CEA) (clone II-7, Dako, dilution 1:50), CD10 (clone 56C6, Novocastra, dilution 1:100), CD15 (clone BY87, Novocastra, dilution 1:20), neuron specific enolase (NSE) (clone BBS/NC/VI-H14, Dako, dilution 1:100), chromogranin (clone 5H7, Novocastra, dilution 1:200), synaptophysin (clone SY38, Dako, 1:20) and also against S100 protein (polyclonal, Dako, dilution 1:400). All specimens were counterstained with Meyer's Hematoxylin, examined, and photographed with a Nikon Eclipse 600 microscope.

For negative control, the identical procedure was performed without the primary antibody. As positive

controls, we applied the same method on different human specific tissues known to be positive for the aforementioned antibodies.

Results

At macroscopy, the tumor was well-circumscribed, friable, tan white with yellowish small areas, uniform cut surface and measured approximately 6.5×6.5×6.5 cm. Although such tumors may present areas of hemorrhage and necrosis, these were not observed in our case.

Microscopically, the tumor was composed of bland cuboidal cells, with moderate slightly eosinophilic cytoplasm, arranged in tightly packed, small, elongated tubules and long cords making abrupt transitions to spindle cell morphology, separated by pale or basophilic, mucinous or myxoid appearing stroma (Figure 1); such an appearance is quite common for this entity. Nuclear pleomorphism was absent in both cuboidal and spindle cells (Figure 1). The nuclei were spherical or oval, with small chromatin clumps and small nucleoli (Figure 2).

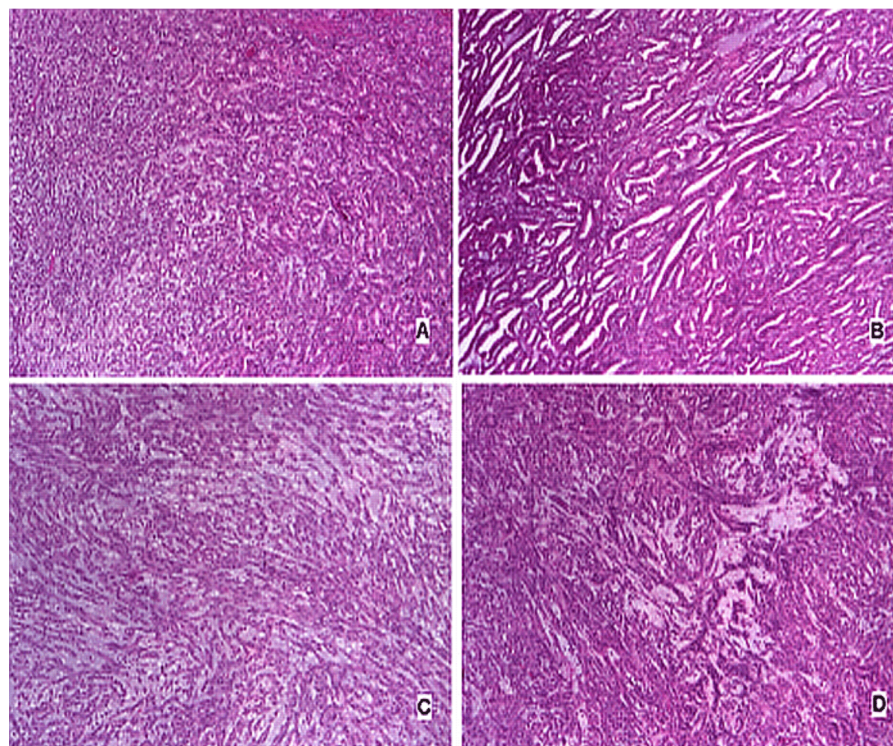


Figure 1 – Mucinous tubular and spindle cell carcinoma – architectural details on HE stain: (A) Tubular arrangement of epithelial cells (×40); (B) Detail of tubular structures (×100); (C) Mucinous material among the tubules and spindle cells (×40); (D) Tumoral cells with cubical and fusiform shape; foam cell deposits (×40).

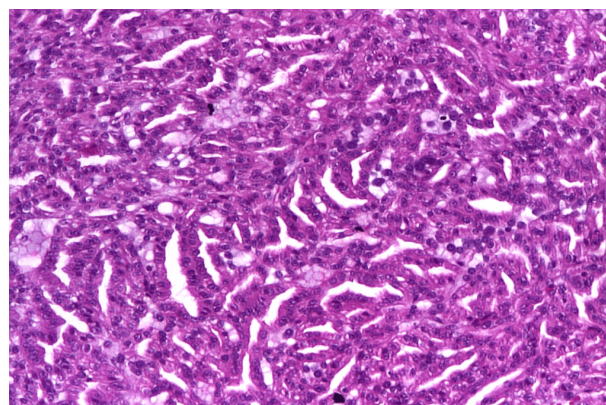


Figure 2 – Mucinous tubular and spindle cell carcinoma: nuclear details (HE stain, ×200).

Mitotic figures were not encountered. The background material strongly reacted with Alcian Blue and PAS (Figure 3) stains, which confirmed its mucinous nature. Intratumoral mononuclear inflammatory infiltrates with focal foamy histiocytes were also noted. We identified a small area of chronic granulomatous inflammatory reaction with foreign-body-type multinucleated giant cells, as well as multifocal foam cell deposits and psammomatous calcifications (Figure 4). Occasionally, areas of necrosis may be found [3]; our case showed no such areas. Papillary areas and cysts were not identified. There was no invasion of the renal capsule or of the perihilar fat.

Immunohistochemical testing performed in this case revealed most of the tumoral cells of the tubular

epithelial component showed diffuse positive cytoplasmic reaction with antibodies against cytokeratin 7 (Figure 5) and also diffuse positive membrane and cytoplasmic reaction for epithelial membrane antigen (Figure 6). The spindle cell component in the tumor reacted intensely with antibodies against vimentin in the cytoplasm. Testing for CD10, CD15, CEA, S100

protein and neuroendocrine markers (neuron specific enolase, chromogranin, synaptophysin) turned out negative in tumoral cells.

Considering the microscopic morphology and the immunohistochemical profile, the case was signed out as mucinous tubular and spindle cell carcinoma.

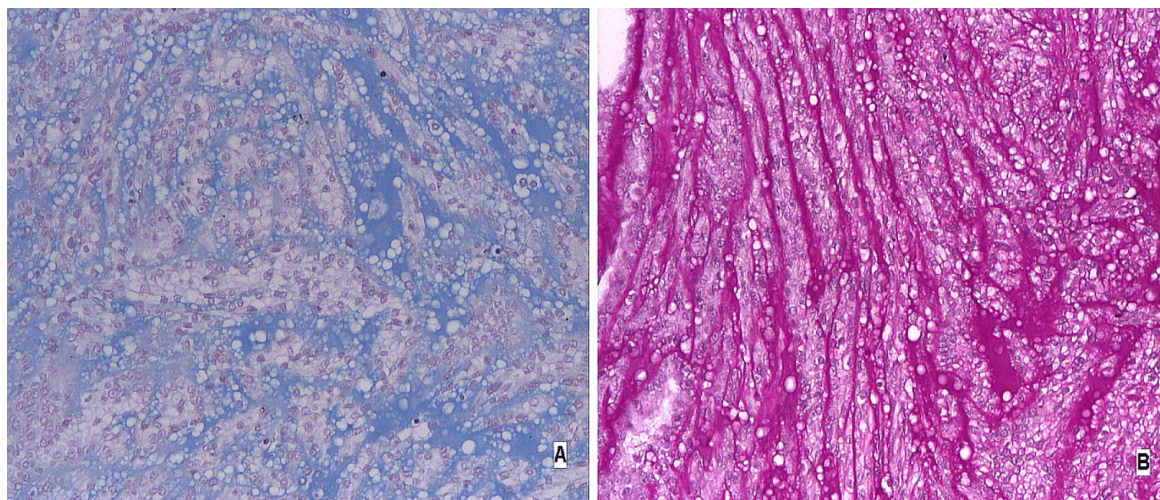


Figure 3 – Mucinous tubular and spindle cell carcinoma – special stain positivity for mucin production: (A) Alcian Blue stain (×100), (B) Periodic Acid–Schiff stain (×100).

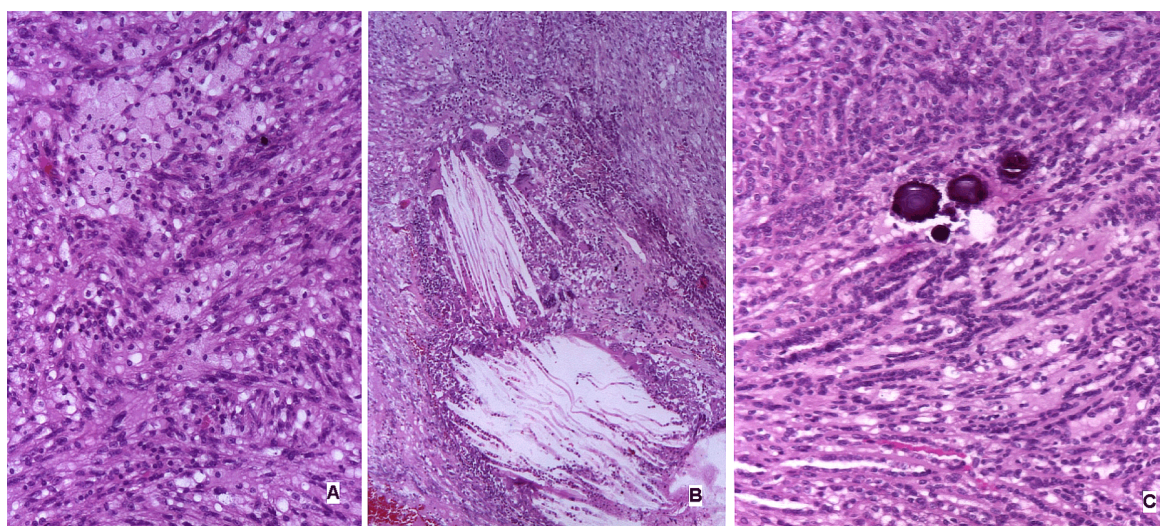


Figure 4 – Mucinous tubular and spindle cell carcinoma – special structural features: (A) Foam cell deposits (HE stain, ×100); (B) Foreign body giant cell reaction (HE stain, ×40); (C) Psammoma-like calcifications (HE stain, ×40).

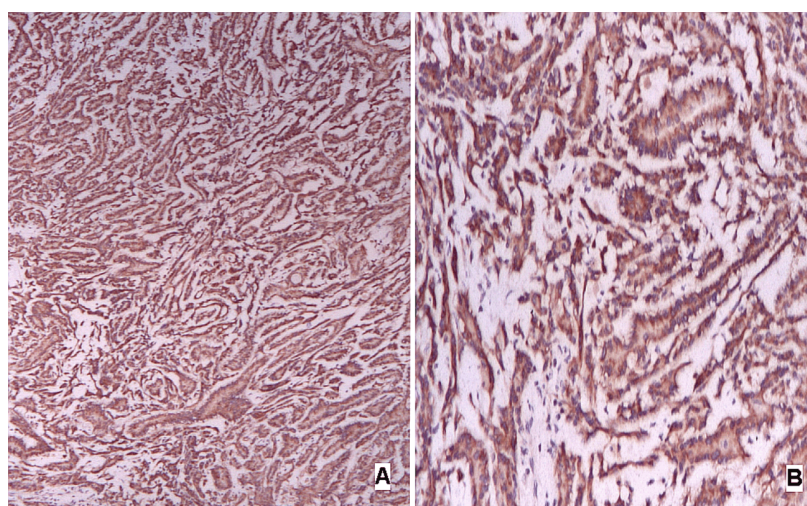


Figure 5 – Mucinous tubular and spindle cell carcinoma – immunohistochemical features: (A) Diffuse positivity of tumoral cells for cytokeratin 7 (×40), and (B) detail (×100).

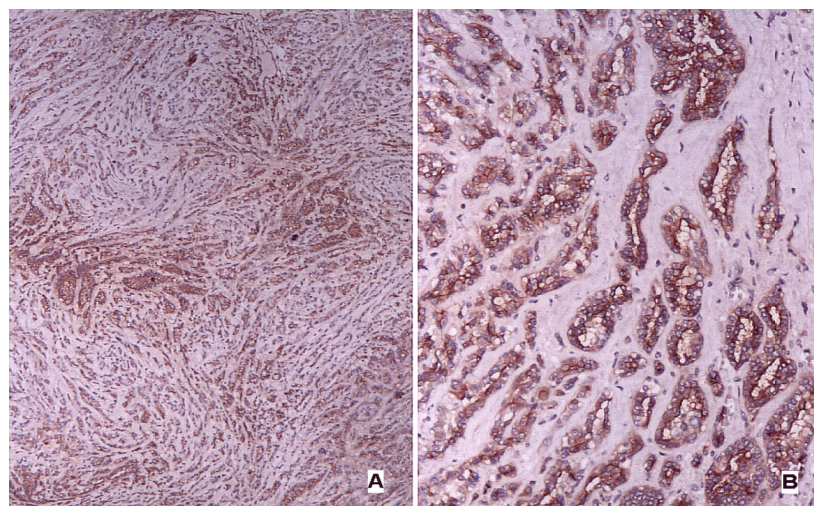


Figure 6 – Mucinous tubular and spindle cell carcinoma – immunohistochemical features: (A) Diffuse positivity of tumoral cells for epithelial membrane antigen ($\times 40$), and (B) detail ($\times 100$).

Discussion

Mucinous tubular and spindle cell carcinoma is a complex type of tumor of relatively recent date recognition, with rare occurrence. Usually, it grows silently and is discovered incidentally, with a definite predominance in female patients (M:F 1:4) [3].

The uncommon morphology of mucinous tubular and spindle cell carcinoma generated a lot of confusion in the past. The tubular architecture showing focal papillae are strong clues pointing to papillary renal cell carcinoma. In cases with predominant spindle cell configuration, mucinous tubular and spindle cell carcinoma can simulate leiomyoma or even sarcoma [2, 3]. Many of these tumors have been previously diagnosed as unclassified or spindle cell (sarcomatoid) carcinomas [3]. Certain key aspects should be underlined since they are particularly important in making a differential diagnosis:

- mucinous tubular and spindle cell carcinoma is usually a circumscribed, biphasic tumor showing an epithelial component as compressed tubules and/or cords [7–9], with more or less obvious mucinous production, and a spindle cell component [10, 11];
- usually there is a rich inflammatory infiltrate with lymphocytes and plasma cells, and no necrosis;
- tumoral cells lack atypia, nucleoli are inconspicuous and there are no mitoses [7, 12, 13].

Differential diagnosis includes: (1) type 1 and 2 papillary renal cell carcinomas – although resemblances with mucinous tubular and spindle cell carcinoma are many, papillary renal cell carcinoma does not show extracellular mucin, but has specific cytogenetic alterations; (2) papillary renal cell carcinoma with sarcomatoid dedifferentiation – shows atypical, large and polygonal cells, occasionally with clear cytoplasm due to the accumulation of glycogen and lipids, opposed to mucinous tubular and spindle cell carcinoma, in which spindle cells are arranged in parallel bundles with eosinophilic cytoplasm and low-grade nuclei [7, 8]; (3) metanephric adenoma – appears as a cellular blue tumor on microscopy, it presents predominant papillary architecture, calcospherites, myxoid stroma, and cells have less cytoplasm; (4) sarcomatoid renal cell carcinomas – may be composed of uniform tumoral

spindle cells but always with areas of considerable nuclear pleomorphism and mitotic activity, which is absent in mucinous tubular and spindle cell carcinomas); (5) collecting duct carcinomas (papillary variant) – tumoral cells are large, eosinophilic, with important cytonuclear atypia in the tubular component; (6) angio-myolipomas – these are smooth muscle cells proliferations, positive for specific markers.

In mucinous tubular and spindle cell carcinoma, the tumoral cells present a complex immunophenotype [11, 14], expressing epithelial markers (CK19, CK7, AE1/AE3) and distal renal tubule markers (EMA, CK19, E-cadherin). Our case presented positive reactions in tumoral cells of the tubular epithelial component for antibodies against cytokeratin 7 and EMA, which is in contrast with metanephric adenoma. Mucinous tubular and spindle cell carcinoma is negative or rarely positive for CD15, CK20, *Ulex europaeus* lectin, CD10, aquaporin 1 [2]; the negativity for CD10 and aquaporin 1 rule out the origin in proximal renal tubules [15]. Neuroendocrine differentiation (positivity for neuron specific enolase, chromogranin, synaptophysin) has been reported in a minority of cases.

The immunohistochemical profile is similar with that encountered in papillary carcinoma, existing the hypothesis that mucinous tubular and spindle cell carcinoma is actually a variant of papillary carcinoma. The morphological interpretation remains an important tool in the distinction between these tumors. At molecular level, an important distinction is that cytogenetic aberrations commonly seen in papillary renal cell carcinomas are not encountered in mucinous tubular and spindle cell carcinoma [6, 16]. Genetic abnormalities found in mucinous tubular and spindle cell carcinomas are monosomies in chromosomes 1, 4, 6, 8, 13, and total or partial trisomies of chromosomes 7, 11, 16, 17.

If compared to other subtypes of renal cell carcinoma, mucinous tubular and spindle cell carcinoma shows reduced aggressiveness and favorable prognosis [17]. These tumors are generally of low pathologic stage at the time of excision, behaving in an indolent fashion. There are extremely rare cases with metastases to lymph nodes and other organs at the time of diagnosis [18]. Only two cases have been reported with metastasis during follow-up as long as 24 years; no tumor related

deaths have been reported [2]. This tumor is best considered as a low-grade carcinoma [3].

✉ Conclusions

Mucinous tubular and spindle cell carcinoma is a rare, recently described, unique subtype of renal cell carcinoma. It must be differentiated from other renal cell carcinomas, which have a much poorer prognosis. Immunohistochemical and cytogenetic studies would be helpful in the diagnosis of this neoplasm. We report this case for its rarity and the complex diagnosis.

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Corresponding author

Alina Grigore, MD, Senior pathologist, Researcher, PhD student, Department of Pathology, “Victor Babeș” National Institute, 99–101 Independenței Avenue, Sector 5, 050096 Bucharest, Romania; Phone +40723–432 134, e-mail: georgescu.alina@gmail.com

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